

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
obert M. Townsend et al.
9/877,987
une 8, 2001

Applicant:

Robert M. Townsend et al.

Serial No.:

09/877,987

Filed:

June 8, 2001

Docket:

D0009NP/30436.53USU1

Title:

METHODS FOR REGULATING A CELL-MEDIATED IMMUNE RESPONSE BY BLOCKING LYMPHOCYTIC SIGNALS AND BY BLOCKING LFA-1 MEDIATED

**ADHESION** 

**CERTIFICATE UNDER 37 CFR 1.8** 

I hereby certify that this paper or fee is being deposited with the United States Postal as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231 on October 26, 2001.

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

We are transmitting herewith the attached:

Transmittal sheet, in duplicate, containing Certificate under 37 CFR 1.8.

Information Disclosure Statement (37 C.F.R. §1.97 (b))

Form 1449 (Information Disclosure Statement) (4 sheets)

Exhibits 1 - 52

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MANDEL & ADRIANO

35 No. Arroyo Parkway, Suite 60 Pasadena, California 91103 (626)395-7801

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

TECH Robert M. Townsend et al.

Examiner:

Not Yet Known

Serial No.:

09/877,987

**Group Art Unit:** 

1645

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June 8, 2001

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**BLOCKING LFA-1 MEDIATED ADHESION** 

**CERTIFICATE UNDER 37 CFR 1.8:** 

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 2023 I on October 26, 2001.

By: Richelle Ann Domingo

INFORMATION DISCLOSURE STATEMENT (37 C.F.R. §1.97(b))

Assistant Commissioner for Patents Washington, D.C. 20231

Dear Sir:

With regard to the above-identified application, the items of information listed on the enclosed Form 1449 are brought to the attention of the Examiner. They are as follows:

- WO 95/33770, December 14, 1995. (Exhibit 1)
- Armitage, Richard J. et al., "Molecular and Biological Characterization of a Murine Ligand for CD40," Letters to Nature, May 7, 1992, 357:80-2. (Exhibit 2)
- Aruffo, Alejandro and Brian Seed, "Molecular Cloning of a CD28 cDNA by a High-Efficiency COS Cell Expression System," Proc. Nat'l Acad. Sci., USA, December 1987, 84:8573-7. (Exhibit 3)

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- Azuma, Haruhito et al., "Blockade of T-Cell Costimulation Prevents Development of
  Experimental Chronic Renal Allograft Rejection," Proc. Nat'l. Sci. Acad. USA, October
  1996, 93:12439-44. (Exhibit 4)
- Blazar, Bruce R. et al., "Coblockade of the LFA1:ICAM and CD28/CTLA4:B7 Pathways Is
   A Highly Effective Means of Preventing Acute Lethal Graft-Versus-Host Disease Induced by
   Fully Major Histocompatibility Complex-Disparate Donor Grafts," Blood, May 1, 1995,
   85(9):2607-18. (Exhibit 5)
- Brunet, Jean-François et al., "A New Member of the Immunoglobulin Superfamily-CTLA-4,"
   Nature, July 16, 1987, 328:267-70. (Exhibit 6)
- Ciubotariu, Rodica et al., "Specific Suppression of Human CD4<sup>+</sup> Th Cell Responses to Pig
   MHC Antigens by CD28<sup>+</sup> CD28<sup>-</sup> Regulatory T Cells," The American Association of Immunologists, 1998, 161:5193-5202. (Exhibit 7)
- Daikh, David et al., "The CD28-B7 Costimulatory Pathway and Its Role in Autoimmune Disease," *Journal of Leukocyte Biology*, August 1997, 62:156-62. (Exhibit 8)
- Damle, Nitin K. et al., "Costimulation of T Lymphocytes with Integrin Ligands Intercellular Adhesion Molecule-1 or Vascular Cell Adhesion Moleucle-1 Induces Functional Expression of CTLA-4, a Second Receptor for B7," *Journal of Immunology*, 1994, 152:2686-97. (Exhibit 9)
- DeBenedette, Mark A. et al, "Costimulation of CD28 T Lymphocytes by 4-1BB Ligand,"
   The Journal of Immunology, 1997, 158:551-9. (Exhibit 10)

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- Deeths, Matthew J. and Matthew F. Mescher, "ICAM-1 and B7-1 Provide Similar But Distinct Costimulation For CD28<sup>+</sup> T Cells, While CD4<sup>+</sup> Cells are Poorly Costimulated by ICAM-1," Eur. J. Immunol., 1990, 29:45-53. (Exhibit 11)
- Dong, Haidong et al., "B7-H1, A Third Member of the B7 Family, Co-Stimulates T-Cell Proliferation and Interleukin-10 Secretion," *Nature Medicine*, <u>December 1999</u>, 5(12):1365-9.
   (Exhibit 12)
- Dubey, Caroline and Michael Croft, "Accessory Molecule Regulation Naïve CD4 T Cell Activation," *Immunologic Research*, 1996, 15:114-25. (Exhibit 13)
- Glysing-Jensen, Troels et al., "Chronic Blockade of CD28-B7-Mediated T-Cell Costimulation by CTLA4Ig Reduces Intimal Thickening in MHC Class I and II Incompatible Mouse Heart Allografts," *Transplantation*, <u>December 27, 1997</u>, 64(12):1641-5. (Exhibit 14)
- Grabstein, Kenneth H. et al., "The Regulation of T Cell-Dependent Antibody Formation in Vitro by CD40 Ligand and IL-2," *The Journal of Immunology*, <u>April 15, 1993</u>, 150(8):3141-7. (Exhibit 15)
- Graf, Daniel et al., "Cloning of TRAP, a ligand for CD40 on Human T Cells," Eur. J. Immonol., 1992, 22:3191-4. (Exhibit 16)
- Green, Jonathan M. and Craig B. Thompson, "Modulation of T Cell Proliferative Responses by Accessory Cell Interactions," *Immunologic Research*, 1994, 13:3234-43. (Exhibit 17)
- Greenfield, Edward A. et al., "CD28/B7 Constimulation: A Review," Critical Reviews in Immunology, 1998, 18:389-418. (Exhibit 18)

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• Hardy, R.R, "Chapter 13: Purification and Characterization of Monoclonal Antibodies,"

Handbook of Experimental Immunology, 1986, 13.1-.13. (Exhibit 20)

• Harper, Katherine et al., "CTLA-4 and CD28 Activated Lymphocyte Molecules are Closely

Related in Both Mouse and Human as to Sequence, Message Expression, Gene Structure and

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• Hathcock, Karen S. et al., "Identification of an Alternative CTLA-4 Ligand Costimulatory for

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• Hollenbaugh, Diane et al., "The Human T Cell Antigen gp39, a Member of the TNF Gene

Family, is a Ligand for the CD40 Receptor: Expression of a Soluble Form of gp39 with B

Cell Co-Stimulatory Activity," *The EMBO Journal*, 1992, 11(12):4313-21. (Exhibit 23)

• Hurtado, Jose C. et al., "Signals Through 4-1BB Are Costimulatory to Previously Activated

Splenic T Cells and Inhibit Activation-Induced Cell Death," The Journal of Immunology,

1997, 158:2600-9. (Exhibit 24)

• Hutloff, Andreas et al, "ICOS is an Inducible T-Cell Co-Stimulator Structurally and

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- Isobe, Mitsuaki et al., "Acceptance of Primary Skin Graft After Treatment with Anti-Intrecellular Adhesion Molecule-1 and Anti-Leukocyte Function-Associated Antigen-1 Monoclonal Antibodies in Mice," *Transplantation*, August 15, 1996, 62(3):411-3. (Exhibit 26)
- Isobe, Mitsuaki et al., "Regulation by Differential Development of Th1 and Th2 Cells in Peripheral Tolerance to Cardiac Allograft Induced by Blocking ICAM-1/LFA-1 Adhesion," *Circulation*, 1997, 96:2247-53. (Exhibit 27)
- Isobe, Mitsuaki et al., "Specific Acceptance of Cardiac Allograft After Treatment with Antibodies to ICAM-1 and LFA-1," *Science*, February 1992, 255:1125-7. (Exhibit 28)
- Judge, Thomas A. et al., "The In Vivo Mechanism of Action of CTLA4Ig," The American
   Association of Immunologists, 1996, 156:2294-9. (Exhibit 29)
- Judge, Thomas A. et al., "The Role of CD80, CD86 and CTLA4 in Alloimmune Responses and the Induction of Long-Term Allograft Survival," The American Association of Immunologists, 1999, 162:1947-51. (Exhibit 30)
- June, Carl H. et al., "The B7 and CD28 Receptor Families," Immunology Today, 1994,
   15(7):321-31. (Exhibit 31)
- Keizer, Gerrit D. et al., "Biochemical and Functional Characteristics of the Human Leukocyte Membrane Antigen Family LFA-1, Mo-1 and p150,95\*," Eur. J. Immunol., 1985, 15:1142-7.
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- Kim, Jong J. et al., "Intracellular Adhesion Molecule-1 Modulates β-Chemokines and Directly Costimulates T Cells In Vivo," The Journal of Clinical Investigation, March 1999, 103(6):869-77. (Exhibit 33)
- Kirk, Allan D. et al., "CTLA4-Ig and Anti-CD40 Ligand Prevent Renal Allograft Rejection in Primates," Proc. Nat'l. Acad. Sci. USA, August 1997, 94:8789-94. (Exhibit 34)
- Konieczny, Bogumila T. et al., "IFN-y is Critical for Long-Term Allograft Survival Induced by Blocking the CD28 and CD40 Ligand T Cell Costimulation Pathways," The Journal of *Immunology*, 1998, 160:2059-64. (Exhibit 35)
- Larsen, Christian P. et al., "CD40-gp39 Interactions Play a Critical Role During Allograft Rejection," Transplantation, January 15, 1996, 61(1):4-9. (Exhibit 36)
- Larsen, Christian P. et al., "Long-Term Acceptance of Skin and Cardiac Allografts After Blocking CD40 and CD28 Pathways," Nature, May 30, 1996, 381:434-8. (Exhibit 37)
- Lenschow, Deborah J. et al., "CD28/B7 System of T Cell Costimulation," Annu. Rev. Imuunol., 1996, 14:233-58. (Exhibit 38)
- Lenschow, Deborah J. et al., "Long-Term Survival of Xenogeneic Pancreatic Islet Grafts Induced by CTLA4Ig," Science, August 7, 1992, 257:789-92. (Exhibit 39)
- Linsley, Peter S. et al, "CTLA-4 is a Second Receptor for the B Cell Activation Antigen B7," J. Exp. Med., September 1991, 174:561-8. (Exhibit 40)
- Linsley, Peter S. et al., "Immunosuppression in Vivo by a Soluble Form of the CTLA-4 T Cell Activation Molecule," Science, August 7, 1992, 257:792-5. (Exhibit 41)

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- Miwa, Shiro et al., "Effect of Anti-Intercellular Adhesion Molecule-1 and Anti-Leukocyte
  Function Associated Antigen-1 Monoclonal Antibodies on Rat-to-Mouse Cardiac Xenograft
  Rejection," Surgery, June 1997, 121(6):681-9. (Exhibit 42)
- Ni, Hsiao-Tzu et al., "Signaling Pathways Activated by Leukocyte Function-Associated Ag 1-Dependent Costimulation," The Journal of Immunology, 1999, 162:5183-9. (Exhibit 43)
- Niimi, Masanori et al., "The Role of the CD40 Pathway in Alloantigen-Induced
   Hyporesponsiveness In Vivo," The Journal of Immunology, 1998, 161:5331-7. (Exhibit 44)
- Russell, Mary E. et al., "Chronic Cardiac Rejection in the LEW to F344 Rat Model Blockade of CD28-B7 Costimulation by CTLA4Ig Modulates T Cell And Macrophage Activation and Attenuates Arteriosclerosis," J. Clin. Invest., February 1996, 97(3):833-8. (Exhibit 45)
- Shimizu, Yoji et al., "Roles of Adhesion Molecules in T-Cell Recognition: Fundamental Similarities Between Four Integrins on Resting Human T Cells (LFA-1, VLA-4, VLA-5, VLA-6) in Expression, Binding and Costimulation," *Immunological Reviews*, 1990, 114:109-43. (Exhibit 46)
- Sun, Hong et al., "Prevention of Chronic Rejection in Mouse Aortic Allografts by Combined Treatment with CTLA4-Ig and Anti-CD40 Ligand Monoclonal Antibody," *Transplantation*, December 12, 1997, 64(12):1838-56. (Exhibit 47)
- Tan, Rusung et al., "B7 Costimulates Proliferation of CD4<sup>-</sup>8<sup>+</sup> T Lymphocytes But Is Not Required for the Deletion of Immature CD CD4<sup>-</sup>8<sup>+</sup> Thymocytes," *The Journal of Immunology*, November 15, 1992, 149(10):3217-24. (Exhibit 48)

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• Tang, Aimin et al., "Blockade of CD40-CD40 Ligand Pathway Induces Tolerance in Murine

Contact Hypersensitivity," Eur. J. Immunol., 1997, 27:3143-50. (Exhibit 49)

Trambley, Joel et al., "Asialo GM1<sup>+</sup> CD8<sup>+</sup> T Cells Play a Critical Role in Costimulation

Blockade-Resistant Allograft Rejection," The Journal of Clinical Investigation, December

1999, 104:1715-22. (Exhibit 50)

• Van Gool, Stefaan W. et al., "CD80, CD86 and CD40 Provide Accessory Signals in a

Multiple-Step T-Cell Activation Model," Immunological Reviews, 1996, 153:47-83. (Exhibit

51)

• Yoshinaga, Steven K. et al., "T-Cell Co-Stimulation Through B7RP-1 and ICOS," Nature,

December 16, 1999, 402:327-32. (Exhibit 52)

This statement should be considered because it is submitted before the mailing date of the first

Office Action on the merits. In accordance with 37 C.F.R. §1.98(a), copies of each document or

other information listed on the enclosed Form 1449 are provided.

No representation is made that a reference is "prior art" within the meaning of 35 U.S.C. §§ 102

and 103 and Applicants reserve the right, pursuant to 37 C.F.R. § 1.131 or otherwise, to establish

that the reference(s) are not "prior art." Moreover, Applicants do not represent that the

references have been thoroughly reviewed or that any relevance of any portion of a reference is

intended.

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Page 9

Consideration of the items listed is respectfully requested. Pursuant to the provisions of

M.P.E.P. 609, it is requested that the Examiner return a copy of the attached Form 1449, marked

as being considered and initialed by the Examiner, to the undersigned with the next official

communication.

No fee is deemed necessary in connection with the filing of this Information Disclosure

Statement. However, if any additional fee is required, authorization is hereby given to charge the

amount of any such fee to Deposit Account No. 50-0306.

Respectfully submitted,

Sarah B. Adriano

Registration No. 34,470

Attorney for Applicants

Mandel & Adriano

35 No. Arroyo Parkway, Suite 60

Pasadena, California 91103

(626)395-7801

Customer No.: 26,941

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FORM 1449*	Docket Number	Application Number
	D0009NP/30436.53USU1	09/877,987
OF ENEORMATION DISCLOSURE STATEMENT	Applicant	<del></del>
IN AN APPLICATION	Robert M. Townsend et al.	
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	WO95/33770 (Exhibit 1)	December 14, 1995					<del></del>
	OTHER	DOCUMENTS (Includin	g Author, Title, Da	te. Pertinent Pa	ges. Etc.)		
		ge, Richard J. et al., "Mo				Ligand for	r CD40 "
	Letters	to Nature, May 7, 1992,	357:80-2. (Exhibi	t 2)		_	
	Aruffo,	Alejandro and Brian Se	ed, "Molecular Clo	ning of a CD28	cDNA by a High	-Efficiency	COS
	Cell Ex	pression System," <i>Proc.</i> , Haruhito et al., "Blocka	Nat'l Acad. Sci., U	SA, December 1	987, 84:8573-7.	(Exhibit 3	3) 
	Chroni	c Renal Allograft Rejecti	ion." <i>Proc. Nat'l. Sc</i>	nulation Prevent	s Development o October 1996, 93:	1 Experim 12439-44	entai (Exhibi
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	Blazar,	Bruce R. et al., "Cobloc	kade of the LFA1:I	CAM and CD28	/CTLA4:B7 Path	ways Is A	Highly
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	Ciubota	ariu, Rodica et al., "Spec	ific Suppression of	Human CD4 <sup>+</sup> Tl	n Cell Responses	to Pig MF	IC
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		ol., <u>1990</u> , 29:45-53. (Extended to the control of		the R7 Family (	Co-Stimulates T	Cell Prolif	eration
		erleukin-10 Secretion," A					CI ativii
	Dubey,	Caroline and Michael Caroline	roft, "Accessory Mo	lecule Regulation			ivation,"
	Immuno	ologic Research, <u>1996,</u> 1	5:114-25. (Exhibit	13)			

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

<sup>\*</sup>Substitute Disclosure Statement Form (PTO-1449)

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) PADEMAR Glysing-Jensen, Troels et al., "Chronic Blockade of CD28-B7-Mediated T-Cell Costimulation by CTLA4Ig Reduces Intimal Thickening in MHC Class I and II Incompatible Mouse Heart Allografts," Transplantation, December 27, 1997, 64(12):1641-5. (Exhibit 14) Grabstein, Kenneth H. et al., "The Regulation of T Cell-Dependent Antibody Formation in Vitro by CD40 Ligand and IL-2," The Journal of Immunology, April 15, 1993, I50(8):3141-7. (Exhibit 15) Graf, Daniel et al., "Cloning of TRAP, a ligand for CD40 on Human T Cells," Eur. J. Immonol., 1992, 22:3191-4. (Exhibit 16) Green, Jonathan M. and Craig B. Thompson, "Modulation of T Cell Proliferative Responses by Accessory Cell Interactions," Immunologic Research, 1994, 13:3234-43. (Exhibit 17) Greenfield, Edward A. et al., "CD28/B7 Constimulation: A Review," Critical Reviews in Immunology, 1998, 18:389-418. (Exhibit 18) Griggs, Nathan D. et al., "The Relative Contribution of the CD28 and gp39 Costimulatory Pathways in the Clonal Expression and Pathogenic Acquisition of Self-Reactive T Cells," J. Exp. Med., March 1996, 183:801-10. (Exhibit 19) Hardy, R.R, "Chapter 13: Purification and Characterization of Monoclonal Antibodies," Handbook of Experimental Immunology, 1986, 13.1-.13. (Exhibit 20) Harper, Katherine et al., "CTLA-4 and CD28 Activated Lymphocyte Molecules are Closely Related in Both Mouse and Human as to Sequence, Message Expression, Gene Structure and Chromosomal Location," The Journal of Immunology, August 1, 1991, 147(3):1037-44. (Exhibit 21) Hathcock, Karen S. et al., "Identification of an Alternative CTLA-4 Ligand Costimulatory for T Cell Activation," Science, November 5, 1993, 905-7. (Exhibit 22) Hollenbaugh, Diane et al., "The Human T Cell Antigen gp39, a Member of the TNF Gene Family, is a Ligand for the CD40 Receptor: Expression of a Soluble Form of gp39 with B Cell Co-Stimulatory Activity," The EMBO Journal, 1992, 11(12):4313-21. (Exhibit 23) Hurtado, Jose C. et al., "Signals Through 4-1BB Are Costimulatory to Previously Activated Splenic T Cells and Inhibit Activation-Induced Cell Death," The Journal of Immunology, 1997, 158:2600-9. (Exhibit 24) Hutloff, Andreas et al, "ICOS is an Inducible T-Cell Co-Stimulator Structurally and Functionally Related CD28," Nature, January 1999, 397:263-6. (Exhibit 25) Isobe, Mitsuaki et al., "Acceptance of Primary Skin Graft After Treatment with Anti-Intrecellular Adhesion Molecule-1 and Anti-Leukocyte Function-Associated Antigen-1 Monoclonal Antibodies in Mice," Transplantation, August 15, 1996, 62(3):411-3. (Exhibit 26) lsobe, Mitsuaki et al., "Regulation by Differential Development of Th1 and Th2 Cells in Peripheral Tolerance to Cardiac Allograft Induced by Blocking ICAM-1/LFA-1 Adhesion," Circulation, 1997, 96:2247-53. (Exhibit 27) Isobe, Mitsuaki et al., "Specific Acceptance of Cardiac Allograft After Treatment with Antibodies to ICAM-1 and LFA-1," Science, February 1992, 255:1125-7. (Exhibit 28) Judge, Thomas A. et al., "The In Vivo Mechanism of Action of CTLA4Ig," The American Association of Immunologists, 1996, 156:2294-9. (Exhibit 29) Judge, Thomas A. et al., "The Role of CD80, CD86 and CTLA4 in Alloimmune Responses and the Induction of Long-Term Allograft Survival," The American Association of Immunologists, 1999, 162:1947-51. (Exhibit 30)

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	Kirk, Allan D. et al., "CTLA4-Ig and Anti-CD40 Ligand Prevent Renal Allograft Rejection in Primates," <i>Proc. Nat'l. Acad. Sci. USA</i> , August 1997, 94:8789-94. (Exhibit 34)
	Konieczny, Bogumila T. et al., "IFN-γ is Critical for Long-Term Allograft Survival Induced by Blocking the CD28 and CD40 Ligand T Cell Costimulation Pathways," <i>The Journal of Immunology</i> , 1998, 160:2059-64. (Exhibit 35)
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EXAMINER	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citatif not in conformance and not considered. Include copy of this	tion is in conformance with MPEP 609; draw line through citation s form for next communication to the Applicant.
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FORM 1449*	Docket Number	Application Number
OIPE	D0009NP/30436.53	USU1 09787-7,987
O ' C LECTION DISCLOSURE STATEMENT	Applicant	127
IN AN APPLICATION	Robert MECH GENH	Ethal 600/2000
	Filing Date	Group Art Unit
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·	OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)
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**EXAMINER** 

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<sup>\*</sup>Substitute Disclosure Statement Form (PTO-1449)